

schema for the mechanism, the amino acid chain then separates, binds with other chains, and folds into the protein molecule.

Zamecnik and his collaborators discovered that in preparing microsome fractions, RNA occurred both in the fraction containing ribosomes bound to the endoplasmic reticulum and in the supernatant. They started referring to the RNA in the supernatant as “soluble RNA” or “S-RNA.” Moreover, they found that labeled leucine was taken up by the S-RNA (Zamecnik et al., 1957; for an analysis of the discovery of soluble RNA, see Rheinberger, 1997). Smith, Cordes, and Schweet (1959) introduced the name “transfer RNA” (tRNA) for S-RNA, and proposed that it played a role in transferring the activated amino acid to the microsomal RNA, a suggestion Zamecnik readily adopted (Hoagland, Zamecnik, & Stephenson, 1959). The notion of transfer also suggests a role for this RNA in sequencing of amino acids, a suggestion that Zamecnik began to formulate:

We have most lately been concerned with the possibility that at least a portion of the soluble RNA molecule to which the amino acid is attached is transferred along with the amino acid to the ribonucleoprotein particle, aligning itself in some base-pairing arrangement with the microsomal RNA prior to formation of a peptide chain. This concept agrees with the proposal of Crick that the soluble RNA molecule may serve as an adaptor in a base-pairing arrangement which determines amino acid sequence. (1958–9, p. 274)

As Zamecnik conceived the mechanism at this point, ribosomal RNA remained in place to direct multiple iterations of synthesis. The tRNA brought amino acids to the template as specified; the amino acids were added to the chain; and the tRNA departed. This made sense in eukaryote cells whose synthetic activities were limited to a few specific proteins. Research on bacteria generated a very different picture, for bacterial cells are capable of generating a wide range of proteins. Especially after the Pardee, Jacob, and Monod (1959) experiment showing the inducibility of protein synthesis, attention refocused on how temporary structures could be made from DNA, then move to the cytoplasm to direct protein synthesis (Brenner, Jacob, & Meselson, 1961). Investigations by Nirenberg and Matthaei (1961) that were directed toward developing a cell-free system for performing protein synthesis revealed that synthetic RNA created with uracil resulted in the synthesis of amino acid chains comprised of phenylalanine. Although this research is most celebrated for providing the first clue to the genetic code, it also provided compelling evidence for a third form of RNA, which came to be known as *messenger RNA* (*mRNA*), which was credited with carrying information about the protein to be synthesized from the nucleus to the ribosome.